Infant Survival, HIV Infection, and Feeding Alternatives in Less-Developed Countries

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ABSTRACT

Objectives. This study examines, in the context of the human immunodeficiency virus (HIV) epidemic, the effects of optimal breast-feeding, complete avoidance of breast-feeding, and early cessation of breast-feeding.

Methods. The three categories of breast-feeding were weighed in terms of HIV transmission and infant mortality. Estimates of the frequency of adverse outcomes were obtained by simulation.

Results. Avoidance of all breast-feeding by the whole population always produces the worst outcome. The lowest frequency of adverse outcomes occurs if no HIV-seropositive women breast-feed and all seronegative women breast-feed optimally, given infant mortality rates below 100 per 1000 and relative risks of dying set at 2.5 for non–breast-fed compared with optimally breast-fed infants. For known HIV-seropositive mothers, fewer adverse outcomes result from early cessation than from prolonged breast-feeding if the hazard of HIV transmission through breast-feeding after 3 months is 7% or more, even at high mortality rates, given relative risks of dying set at 1.5 for early cessation compared with optimal duration of breast-feeding.

Conclusions. The risk of HIV transmission through breast-feeding at various ages needs to be more precisely quantified. The grave issues that may accompany a possible decline in breast-feeding in the less developed world demand evaluation. (*Am J Public Health.* 1997;87:926–931)

Introduction

For some time, pediatricians in North America and Europe have followed formal guidelines that discourage breast-feeding for women with human immunodeficiency virus (HIV) infection.[1] World Health Organization guidelines recommend just the opposite for women in developing countries.[2] Both of these contradictory policies gloss over a complex set of observations critical to infant feeding policies wherever the epidemic rages. For the developing world, enough is known to call into question any single overarching recommendation.

Breast-feeding can undoubtedly transmit HIV infection from an infected mother to her uninfected infant. One meta-analysis attributed to breast-feeding a 14% excess risk (95% confidence interval [CI] = 7%, 21%).[3] At the same time, failure to breast-feed adds to the risks of diarrheal disease, other infectious diseases, poor growth and development, and infant mortality.[4–6]

A central concern of this paper is the contribution of the duration of breast-feeding. In the studies included in the meta-analysis cited above, the median duration of breast-feeding was short (4 to 8 weeks),[3] which points to a high risk of HIV transmission in the first few weeks of breast-feeding. However, there may also be substantial risks of HIV transmission with prolonged breast-feeding. Some children of HIV-infected women born HIV antibody positive have seroreverted to become antibody negative, but later, while being breast-fed, seroconverted.[7–10] In one study, 18% of children of HIV-infected women manifested this antibody pattern.[9] Other studies have been able to detect HIV DNA up to 12 months postpartum in milk samples of about one third to one half of HIV-infected women.[11,12] The beneficial effects of breast-feeding are almost certainly greatest in the first few months of life and decline as the child becomes older and other foods are introduced.[13]

In this paper, we model the expected frequency of adverse outcomes (HIV infections and infant deaths) associated with different infant feeding practices in the context of the HIV epidemic. We compare complete avoidance of breast-feeding with optimal prolonged breast-feeding (up to 12 months or longer), and, unlike previous models,[14–18] we also compare each of these with early cessation of breast feeding (by 3 months of age). Throughout, we consider the implications for known HIV-seropositive women and for women who do and those who do not know their serostatus.

Methods

Adverse Outcomes

We estimate the number of adverse outcomes expected to occur, given different infant feeding practices, in simulations. Adverse outcomes are either HIV infections or deaths in the first year of life.

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Both are counted as equivalent outcomes to be minimized by infant feeding policies. Thus, HIV infection is presumed to be untreated and fatal in childhood, although it is now known that a few infected children survive even to adolescence.

Knowledge of HIV Status

HIV status may be known by few women. These include those served by select hospitals and clinics (mostly urban academic centers, or rural research settings that offer counseling, testing, and disclosure of serostatus to pregnant women); perhaps also those who have had a previous infant with recognized HIV infection; and women with advanced disease.

We estimate the expected frequency of adverse outcomes in two situations. In one, the HIV status of individual women is unknown and thus infant feeding practices would be the same among all women regardless of HIV serostatus at delivery. In the other, the HIV status of women is known and thus feeding practices can be allowed to differ according to positive or negative HIV status at delivery.

Testing and disclosure policies may of course change and especially if low-priced and effective antiretroviral drugs to reduce perinatal HIV transmission become widely available.

Infant Feeding Practices

First, we compare outcomes for all women (regardless of HIV serostatus) under three conditions: if they breast-feed their infants optimally (exclusive breast-feeding to age 4–6 months and breast-feeding supplemented by other foods to 12 months or longer[19]), if they avoid breast-feeding entirely, or if they cease to breast-feed their infants by 3 months of age. Next, we compare outcomes of women who are HIV seropositive at delivery if they avoid breast-feeding entirely or if they cease to breast-feed early, while all women who are seronegative at delivery breast-feed optimally.

Models

The number of adverse outcomes can be modeled as a function of the following parameters:

1. *HIV seroprevalence.* The HIV seroprevalence among parturient women in similar circumstances in the population needs to be taken into account. Prevalence is allowed to vary between 5% and 25%, values that correspond to the range in many developing countries.[20] Surveillance data (e.g., through unlinked serosurveys) already supply this information in many settings, and more may do so as data collection becomes less costly with advances, such as saliva tests and simple rapid assays, in assessing serostatus.

2. *HIV incidence.* The annual postpartum HIV incidence among women who are seronegative at delivery is assumed to be either low (1%) or high (5%). These levels are on the high side, since, for most settings,[21] the contribution from this source is small.

3. *Infant mortality rates.* The infant mortality rates used refer to rates among optimally breast-fed infants of HIV-seronegative women and are allowed to range from 20 to 160 per 1000 live births. Mortality unrelated to HIV is assumed to be the same in infants of HIV-seropositive and seronegative women. Mortality declines in the course of the first year of life.[22] In an exponential model[23] with two thirds of deaths assigned to the first 6 months,[22] 46% of infant deaths occur before 3 months of age. The proportion of early deaths may be higher if the infant mortality rate is lower. As the pre-HIV infant mortality rate among breast-fed infants varies within countries, for generalizing the model, the rate that most closely corresponds to that for the dwelling places and characteristics of the women concerned should be considered.

4. *HIV transmission rates.* We assume that 20% of infants born to HIV-infected women are infected prior to or during birth, and that an additional 14% are infected later through breast-feeding, with a lower bound of 7% and an upper bound of 21%.[3]

If a child is breast-fed for only 3 months, we assume an excess postnatal HIV transmission rate of 7%. We estimate too how large this excess risk needs to be to choose early cessation of breast-feeding over complete avoidance of any breast-feeding. For known HIV-seropositive women, we also estimate the size of the smallest hazard of transmitting HIV through long-lasting breast-feeding needed to favor a choice of early cessation over prolonged breast-feeding. The HIV hazard can be interpreted as the probability of acquiring HIV through breast-feeding after the 3 months of age conditional on survival of the infant free of HIV infection to that age.

For the less common situation where a mother becomes infected in the postnatal period, the assumed transmission rate due to breast-feeding is higher, around 30%,[3] on account of the early viremia peak after infection.

5. *Relative risk of infant death if no or less breast-feeding.* There is no doubt that breast-feeding is ordinarily healthiest for infants, and, in most less developed countries, it is the preferred, most convenient, and most economical practice for mothers. For infants entirely denied the breast compared with optimally breast-fed infants, however, the relative risk of death from all causes in the first year of life is not well described. Our best estimate of 2.5 draws on a well-controlled study in Malaysia, which found a relative risk of 2 (95% CI = 1.8, 2.6).[4] The considerably higher relative risks reported in other studies almost always refer to mortality attributable only to diarrheal disease or to other infections.[6]

The proportion of infant deaths attributable to diarrhea and other infections is likely to be higher where overall mortality is higher. Thus the risk of entirely avoiding breast-feeding, too, is likely to be higher where infant mortality rates are higher. Accordingly, we present a sensitivity analysis, at varying levels of infant mortality, of what relative risks might lead to a choice of breast-feeding over artificial feeding.

We allow the relative risk associated with early cessation of breast-feeding to be 1.5, and estimate a critical value for that relative risk when the hazard of transmitting HIV after 3 months of age (conditional on survival of the infant free of HIV infection to that age) through breast-feeding is 7%. Throughout, we assume that there is no effect of breast-feeding on mortality in the second year of life.

Results

Alternative Feeding Practices and Outcomes

Where no HIV testing is assumed and the HIV status of individual women is unknown, all infants regardless of maternal infection are subject to the same blanket policy (Table 1, columns 1 through 3). Withholding breast-feeding exacts a severe toll, especially but not only in areas of low HIV seroprevalence. Universal early cessation of breast-feeding results in better outcomes than universal optimal breast-feeding where infant mortality rates among breast-fed infants of HIV-seronegative women are

TABLE 1—Estimated Numbers of Adverse Outcomes (HIV Infections and Infant Deaths) per 1000 (n) Resulting from Five Alternative Infant Feeding Practices, Given Different Infant Mortality Rates among Breast-Fed Infants of HIV-Seronegative Women and Different HIV Seroprevalence Rates

		No Individual HIV Testing Required			HIV Testing Required	
Infant Mortality Rate (IMR)/1000	HIV Seroprevalence (p), %	(1) All Breast-Feed ≥12 mo, Y_{BF}	(2) No Breast-Feeding, Y_{AF}	(3) All Breast-Feed ≤3 mo, Y_E	(4) HIV+ Women Avoid Breast-Feeding, Y_{HIV+AF}	(5) HIV+ Women Breast-Feed ≤3 mo, Y_{HIV+E}
20	5	39	60	39	34	36
40	5	59	109	64	55	56
60	5	79	159	89	76	76
80	5	98	208	114	97	96
100	5	118	258	139	118	115
120	5	137	307	164	139	135
140	5	157	357	189	159	155
160	5	177	406	214	180	175
20	15	72	79	65	55	63
40	15	91	127	90	78	82
60	15	110	176	114	101	102
80	15	129	224	138	124	121
100	15	148	273	162	147	141
120	15	167	321	186	170	160
140	15	186	370	210	193	180
160	15	205	418	235	216	200
20	25	106	98	91	77	89
40	25	124	145	115	102	108
60	25	142	193	138	127	128
80	25	160	240	162	152	147
100	25	179	288	185	177	166
120	25	197	335	208	202	186
140	25	215	383	232	227	205
160	25	233	430	255	252	224

Parameters: HIV transmission rate if no breast-feeding (TR_1) = 20%, if breast-fed ≥12 months ($TR_1 + TR_2$) = 34%, if breast-fed ≤3 months ($TR_1 + TR_{<3}$) = 27%; relative risk artificial feeding vs breast-feeding ≥12 months (RR) = 2.5, relative risk breast-feeding ≤3 months vs ≥12 months (RR_E) = 1.5; percent of infant deaths occurring before 3 months of age (%) = 46%; HIV incidence (I) = 1%; and HIV transmission rate among these if any breast-feeding (TR_1) = 30%. Under the alternatives involving HIV testing, all HIV-seronegative women are assumed to breast-feed ≥12 months.

Formulas: $Y_{BF} = np(TR_1 + TR_2) + np(1 - TR_1 - TR_2)IMR + n(1 - p)I.TR_i + n(1 - p)I(1 - TR_i)IMR + n(1 - p)(1 - I)IMR$.

$Y_{AF} = np.TR_1 + np(1 - TR_1)IMR.RR + n(1 - p)IMR.RR$.

$Y_E = np[(TR_1 + TR_{<3}) + (1 - TR_1 - TR_{<3})\ (\%)\ IMR + (1 - TR_1 - TR_{<3})(1 - \%)IMR.RR_W] + n(1 - p)[0.25.I.TR_i + 0.25.I.(1 - TR_i)\ (\%)\ IMR + (1 - [0.25.I])\ (\%)\ IMR + 0.25.I(1 - TR_i)(1 - \%)IMR.RR_E + (1 - [0.25.I])(1 - \%)IMR.RR_W]$.

$Y_{HIV+AF} = np[TR_1 + (1 - TR_1)IMR.RR] + n(1 - p)[I.TR_i + I(1 - TR_i)IMR + (1 - I)IMR]$.

$Y_{HIV+E} = np[(TR_1 + TR_{<3}) + (1 - TR_1 - TR_{<3})\ (\%)\ IMR + (1 - TR_1 - TR_{<3})(1 - \%)IMR.RR_E] + n(1 - p)[I.TR_i + I(1 - TR_i)IMR + (1 - I)IMR]$.

under 60 per 1000 and HIV prevalence is high.

To portray the possible effects of including HIV testing, adverse outcomes are estimated for all HIV-seropositive women if they do not breast-feed (column 4) or if they breast-feed only to 3 months (column 5), given that all women who are seronegative at delivery (including those who acquire HIV infection postpartum) breast-feed to 12 months or longer (Table 1). The models are informative in that they estimate the maximum possible frequency of preventable adverse outcomes.

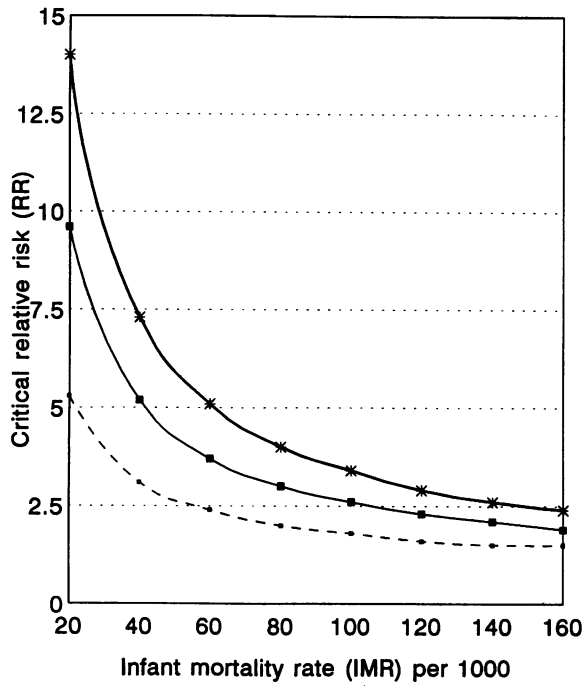
Compared with optimal breast-feeding in the whole population, and given infant mortality under 100 per 1000 live births (among uninfected, breast-fed infants), adverse outcomes are fewer if HIV-seronegative women breast-feed while HIV-seropositive women do not. The reductions are small as long as the population seroprevalence remains low (under 5%), and they rise as prevalence rises. Where HIV prevalence is high (25%) and the infant mortality rate is low (40 per 1000), column 4 strategies command notable advantage.

In Table 1, postnatal HIV incidence in the mother is assumed to be 1%. Comparisons are essentially unchanged if HIV incidence is assumed to be 5% (not shown).

With infant mortality rates of 60 to 100 per 1000, HIV-seropositive women who cease to breast-feed early have fewer adverse outcomes than those who do not breast-feed at all. Sensitivity analyses (not shown) indicate, however, that if the excess risk of an HIV-positive mother's transmitting the virus in the first 3 months of breast-feeding starts to exceed 7%, then complete avoidance of breast-feeding by HIV-seropositive mothers produces fewer adverse outcomes than early cessation of breast-feeding at these levels of infant mortality.

Sensitivity Analysis of Relative Risk

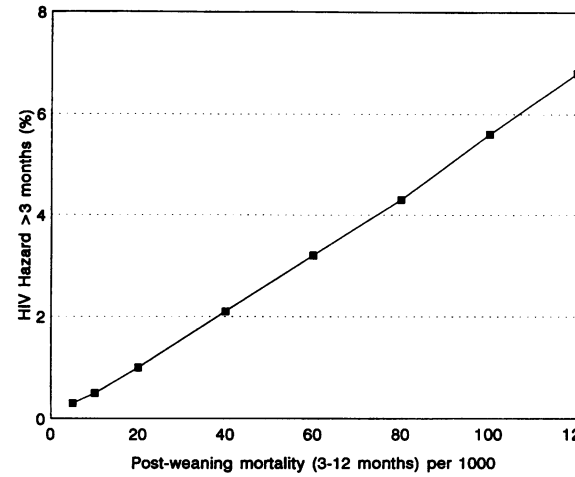
Figure 1 displays the relative risks of no breast-feeding vs optimal breast-feeding in HIV-seropositive women. At lower infant mortality rates among uninfected, breast-fed infants, even if the disadvantage of artificial feeding is quite severe, complete avoidance of breast-feeding results in fewer adverse outcomes than optimal breast-feeding. For instance, at an infant mortality rate under 40 per 1000, the relative risk of dying of all causes during the course of the first year of life has to exceed 3 among never



Note. If the setting-specific relative risk (RR) is greater than the critical value shown, then breast-feeding results in fewer adverse outcomes; if the relative risk is less than the critical value shown, then artificial feeding results in fewer adverse outcomes.

$$RR_{critical} = \frac{TR_2 + (1 - TR_1 - TR_2)IMR}{(1 - TR_1)IMR}$$

FIGURE 1—Choice between breast and artificial feeding for HIV-seropositive women, given different postnatal HIV transmission rates (TR) and infant mortality rates (IMR): the graph shows critical relative risks values due to artificial feeding for different levels of infant mortality.



Note. If, at any given level of post-weaning mortality, the hazard rate (HR) of HIV transmission attributable to breast-feeding longer than 3 months (a conditional probability given HIV-free survival to 3 months) is greater than the critical value, then early cessation of breast-feeding results in fewer adverse outcomes than longer breast-feeding. Relative risk of death due to early cessation of breast-feeding (RR_E) = 1.5 and MR_{3-12} = mortality rate at 3 to 12 months of optimally breast-fed uninfected infants.

$$HR_{>3\ critical} = \frac{MR_{3-12}(RR_E - 1)}{(1 - MR_{3-12})}$$

FIGURE 2—Choice between early cessation of breast-feeding and prolonged breast-feeding for HIV-seropositive women: the graph shows critical values for the hazard of HIV transmission attributable to breast-feeding longer than 3 months, at different levels of post-weaning mortality.

breast-fed compared with optimally breast-fed infants (even at the lower bound of the presumed postnatal HIV transmission rate) before prolonged breast-feeding by known HIV-infected women results in fewer adverse outcomes than complete cessation of breast-feeding. At higher infant mortality rates, only if the disadvantage of artificial feeding is mild (in practice, the disadvantage is likely to increase at higher mortality rates) can artificial feeding result in fewer adverse outcomes than optimal breast-feeding.

Sensitivity Analysis of HIV Transmission Hazard

Figure 2 displays the critical values of the hazard related to early cessation of breast-feeding vs longer breast-feeding in HIV-seropositive women. With 3- to 12-month mortality rates of 50 to 75 per 1000 (which corresponds roughly to an infant mortality rate of 100 per 1000, depending on the distribution of mortality across the first year of life), and the relative risk of infant death associated with early cessation of breast-feeding set at 1.5, early cessation of breast-feeding produces fewer adverse outcomes than prolonged breast-feeding if the hazard of HIV transmission with breast-feeding longer than 3 months is 3% or more. Even at high 3- to 12-month mortality rates, early cessation of breast-feeding produces fewer adverse outcomes than prolonged breast-feeding if the hazard of HIV transmission with breast-feeding longer than 3 months is 7% or more.

Conversely, if the hazard of HIV transmission through breast-feeding longer than 3 months is set at 7%, and the infant mortality rate is less than 120 per 1000, the relative risk of dying after age 3 months associated with removing the infant from the breast at 3 months has to exceed 2 before prolonged breast-feeding by known HIV-infected women results in fewer adverse outcomes than shortened duration of breast-feeding.

Discussion

We demonstrate here that the frequency of adverse outcomes is lower if all HIV-seropositive women do not breast-feed while all seronegative women breast-feed optimally, given infant mortality rates among uninfected breast-fed infants below 100 per 1000 and risks associated with artificial feeding that are moderate but not severe. These conditions may prevail in specific settings in developing countries and are particularly pertinent as HIV seroprevalence rises. Complete avoidance of breast-feeding by the whole population will never be a reasonable option, however, and produces the worst outcomes in almost all circumstances. Thus, if it is not possible to distinguish individual from community risk (e.g., in the absence of HIV testing), sustained promotion of breast-feeding appears to be most desirable.

We demonstrate further that early cessation of breast-feeding at 3 months of age for known HIV-seropositive mothers results in lower frequencies of adverse outcomes than does prolonged breast-feeding even in settings with high infant mortality rates, if the hazard of acquiring HIV infection through breast-feeding after 3 months is 7% or more. Whether complete avoidance of breast-feeding results in fewer adverse outcomes than does early cessation is highly sensitive to age-specific estimates of the risk of HIV transmission through breast-feeding. Thus, the magnitude of these risks needs to be quantified with more precision.

Early cessation of breast-feeding may be a more realistic or desirable alternative in many settings. Shorter breast-feeding may be less stigmatizing and more satisfying to the mother than absolute denial of breast-feeding. It may be possible, with appropriate nutritional advice and support, to avoid the use of feeding bottles and to use locally available or processed foods instead of commercial milk formula. However, it is important that the birth control needs of postpartum women be considered should the natural contraceptive benefits of breast-feeding be lost.

Key parameters in these models may be modified as more precise knowledge accrues or as clinical or socioeconomic factors change. Of particular interest is whether HIV transmission through breast-feeding will be reduced with treatment (with antiretroviral drugs or vitamin A) of mother and infant provided around the time of delivery, or whether reductions in perinatal transmission will offer greater opportunity for postnatal transmission.

Breast-feeding is deeply rooted in tradition in many societies, and for women nearly everywhere it is a highly valued attribute of childbearing and an affirmation of motherhood. If one holds the view, as many do, that infant feeding decisions rest inalienably with the mother, then the information on competing risks should be conveyed to her. But can it be conveyed in a way that is clear, supportive, and nonjudgmental? Implicit too is the need for a policy regarding HIV testing, which also has implications concerned not only with health and economics, but also with the rights of women, as of men, to be protected against stigma and discrimination.

Programs attempting to reduce the risk of HIV transmission through breast-feeding will need to promote and protect breast-feeding among uninfected women[24] as well as devise constructive methods to minimize adverse outcomes associated with artificial feeding. The feasibility, acceptability, safety, and cost of such programs need to be evaluated.

It is urgent that the grave social, economic, and personal issues that may accompany changes in infant feeding practices in the face of the HIV epidemic be explored from new angles. □

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